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Lessons learned from delayed diagnosis in Acute Intermittent Porphyria

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Case report

Lessons learned from delayed diagnosis in Acute Intermittent Porphyria

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Abstract

A 56-year-old, previously healthy woman with a family history of acute intermittent porphyria (AIP) presenting with altered mental status, severe abdominal pain and falls; who later developed seizures and new delusions involving missing organs. Due to the nonspecific clinical presentation of AIP and low availability of diagnostic tools, the diagnosis was delayed resulting in treatment delay. This case report hopes to raise AIP awareness among clinicians, so better care can be delivered.

Key words: porphyria, seizures, acute psychosis, hypertensive emergency, diagnosis and management

Introduction

Acute Intermittent Porphyria (AIP), also known as Swedish porphyria, is an uncommon, inherited disorder of the heme synthesis pathway. It usually presents with episodic, acute neurovisceral attacks that can be life-threatening. The estimated prevalence of acute attack is approximately 5 per 100,000.[1] Diagnosis and management of AIP has been a challenge due to its nonspecific clinical manifestations, low clinical suspicion, and unavailability of diagnostic tools as well as prompt treatment. We report an adult female with a family history of AIP who presented with several days of altered mental status, severe abdominal pain, and falls. In the hospital, she developed seizures, hypertension and symptoms of acute psychosis. AIP diagnosis was presumed later and supported by laboratory findings.

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Case Presentation

A 56-year-old woman with a family history of acute intermittent porphyria (AIP) presented to an outside hospital with a 3-day history of altered mental status, severe abdominal pain and falls. In the Emergency Department, she developed generalized tonic-clonic seizures and hypertensive emergency, requiring intubation and Intensive Care Unit admission. Her condition stabilized following treatment with lorazepam, levetiracetam and labetalol. A brain MRI without contrast showed signs of chronic hypertensive microhaemorrhage without acute intracranial abnormalities. An abdominal ultrasound did not reveal significant findings. On day 4, the patient was extubated and transferred to our hospital for further evaluation due to a suspicious for AIP.

On admission, the patient had retrograde amnaesia and developed new delusions involving missing organs. The neurological examinations showed no focal deficits. No skin blisters were seen on exam. She had abdominal pain which resolved with morphine. Laboratory studies included complete blood count, comprehensive metabolic panel, full toxicology screen, TSH, RPR, vitamin B1, 2, 6, 12, D and E, iron, HIV, prothrombin time and urinalysis, which revealed normal results. No epileptic pattern was seen on EEG. She refused lumbar puncture. Due to suspicion of AIP, urine porphobilinogen (PBG) and

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plasma porphyrins were sent for laboratory testing. The patient's delusions and vital sign instability resolved over the next three days, and the patient was discharged on amlodipine, carvedilol, lisinopril and levetiracetam with close follow-up.

One week following discharge, the results of porphyrin testing were received. Random urine PBG was 32.7 µmol/L (Normal range: 0.0-8.8 µmol/L). The 24hour urine PBG was 67.9 µmol/d (Normal range: 0.0-11.0 µmol/d). Plasma porphyrins were not elevated. Fractionated urinary porphyrins showed that uroporphyrin in 24-hour urine was 17µmol/mol (Normal range: 0-4 µmol/mol), coproporphyrin in 24-hour urine was 8 µmol/mol (Normal range: 0-6 µmol/mol) and coproporphyrin (CP) III was 145 µmol/mol (Normal range: 0-14 µmol/mol). Attempts were made to contact the patient, but were unsuccessful. It was later learned that the patient was readmitted to another hospital for a suspected repeat attack.

Discussion

AIP is an autosomal dominant, low penetrance (~1%) disease resulting from mutation in the hydroxymethylbilane synthase (HMBS) gene that codes for porphobilinogen deaminase (PBGD) protein in the heme synthesis pathway.[2] Symptoms may include abdominal pain, vomiting, constipation, paresis, psychiatric symptoms, pain in limb, head, neck, back or chest, respiratory paralysis, hypertension, tachycardia and convulsion, and are highly variable.[3]Associations with posterior reversible encephalopathy syndrome (PRES), hyponatraemia, and syndrome of inappropriate antidiuretic hormone secretion (SIADH) are also documented.[4,5]

Suspicion for AIP should be raised in a patient with unexplained abdominal pain and/or neuropsychiatric symptoms after ruling out more common causes. Urinary PBG should be obtained; an increased level is sufficient to initiate hemin to alleviate attack severity. Carbohydrate loading is another treatment option but is less effective and carries a potential risk of fatal hyponatremia.[6] Further testing for total and fractionated urinary porphyrin, plasma and fecal porphyria should be sent to differentiate between AIP and other acute porphyrias. Confirmation of the diagnosis is made by identifying decreased erythrocyte PBGD and mutation in HMBS gene.[1]

Diagnosis and management of AIP is clinically challenging due to its nonspecific symptoms. Because of its rarity, clinicians often have a low initial suspicion for AIP. Diagnostic testing is not widely available and may take weeks to know result. Because of these challenges, prompt treatment is often delayed. In patients with a known prior diagnosis of AIP, treatment may be started based on clinical diagnosis of an acute attack. In this case, our diagnosis was limited by unavailability of timely PBG results. Despite hemin therapy is indicated in the setting of attacks of AIP, due to unclear diagnosis and clinical improvement, it was not used in this case. It is unclear whether earlier diagnosis and prompt hemin treatment would have prevented re-hospitalization in this patient.

Conclusion

AIP has a nonspecific presentations. Due to the low clinical suspicion and the unavailability of diagnostic tools, diagnosis in AIP is often delayed resulting in treatment delay. Clinicians need to be aware of AIP symptoms and initiate prompt management.

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